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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,795	02/25/2005	Norihito Ohi	0425-1154PUS1	9627

2292 7590 09/26/2006

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EXAMINER	
NOLAN, JASON MICHAEL	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 09/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/509,795	OHI ET AL.	
	Examiner	Art Unit	
	Jason M. Nolan, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-61* is/are pending in the application.

4a) Of the above claim(s) *1-19 and 24-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,22,23,50 and 53-61* is/are rejected.

7)☒ Claim(s) *21,49,51 and 52* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/29/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-61 are currently pending in the instant application; of which, **Claims 1-19** and **24-48** are withdrawn from consideration as being non-elected subject matter. **Claims 50-61** have been amended and no new claims are presented.

Information Disclosure Statement

The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report have not been considered. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a).

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file: JP 2002-158467 and JP 2003-000153.

Applicant cannot rely upon the foreign priority papers to overcome the 35 USC 102(e) rejection over WO 2003064397, which was published on 8/7/2003, because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Response to Restriction

Applicants' election with traverse of **Group VII, Claims 20-23** and **49-61** is acknowledged. The Examiner also acknowledges the election of species: Example 1052, as a representative compound. Further, Examiner acknowledges Applicants' request for inclusion of at least a process of use, for instance, **Group IX**.

Examiner agrees with Applicant in that **Group VII** should have read " **Claims 20-23**, drawn to products of the Formula III, wherein Ar is C_{6-14} aryl group" and **Claim 50** is grouped with **Group IX**.

As outlined in the previous Office Action of June 6, 2006, the structural moiety common to the invention is not a special technical feature, because it fails to define a contribution over the prior art. Therefore, **Claims 1-61** are not so linked as to form a single general inventive concept and there is a lack of unity of invention. The variables vary extensively and when taken as a whole result in vastly different compounds. Additionally, the vastness of the claimed subject matter, and the complications in understanding the claimed subject matter imposes a serious burden on any examination

of the claimed subject matter. Therefore, since the claims do not relate to a single general inventive concept under PCT Rule 13.1 and lack the same or corresponding special technical features, the claims lack unity of invention and should be limited to a product and a method of use. As a result, the claims lack unity of invention and the restriction requirement is Maintained and Final.

Claim Rejections - 35 USC § 102

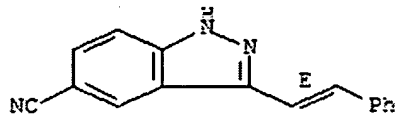
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 20 and 50-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Bhagwat *et al.* (WO 2002010137, published 2002/02/07; priority US Provisional 2000-221799, filed 2000/07/31). Shown below is the compound RN 395102-15-5 and discussed in the Abstract of the Publication is the use of pyrazoles as JNK inhibitors.

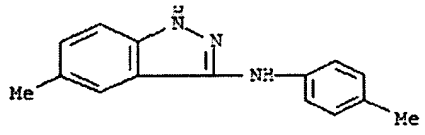
RN 395102-15-5



Claims 20, 50, and 54-61 are rejected under 35 U.S.C. 102(e) as being anticipated by Binch *et al.* (WO 2003064397, published 2003/08/07 and filed on 2003/01/23). Shown in the attached CAS Abstract Search Printout are several compounds in which $\mathbf{R^1}$ is -N(H)Ph (**h**=0, **j**=1, **k**=0), in which the phenyl is substituted or unsubstituted; and **L** is a bond; **X** is –N(H)(CO)-Z, in which **Z** is an optionally substituted $C_{1\text{-}6}$ alkyl. Also included are compounds RN 574729-29-6 and RN 574729-31-0 in which **L** = bond; **X** = bond; and **Y** is nitro. Additionally, in the Abstract of the Publication is described the use of these compounds for the treatment of neurodegenerative disorders.

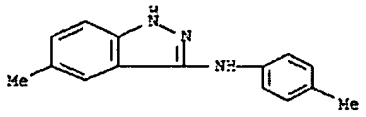
Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Partridge *et al.* (Abstract from Journal of the Chemical Society **1964**, 3663-9). Shown below is the compound RN 840-12-0.

RN 840-12-0

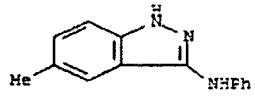


Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Burmistrov *et al.* (Abstract from Khimiya Geterotsiklicheskikh Soedinenii 1973, 2, 249-51). Shown below are the compounds disclosed by Burmistrov that read on said claim.

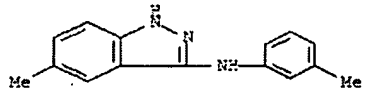
RN 840-12-0 CAPLUS



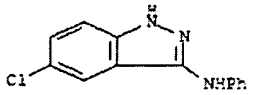
RN 40598-62-7 CAPLUS



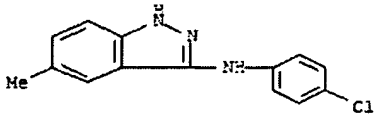
RN 40598-65-0 CAPLUS



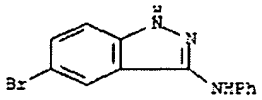
RN 40598-67-2 CAPLUS



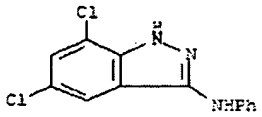
RN 40598-68-3 CAPLUS



RN 40598-69-4 CAPLUS

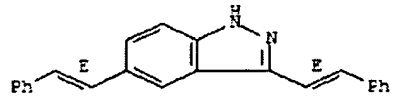


RN 40598-70-7 CAPLUS



Claims 20, 50, 53, 56-57, and 59-60 are rejected under 35 U.S.C. 102(b) as being anticipated by Reich *et al.* (WO 2001053268, published 2001/07/26). Shown below is the compound RN 351454-61-0 and discussed in the Abstract of the Publication is the use of this compound for the treatment of inflammatory diseases such as rheumatoid arthritis.

RN 351454-61-0 CAPLUS



Claim Rejections - 35 USC §§ 101 & 112

Claims 56-58 provides for *the* "use of" compounds of the formula III, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 56-58 are rejected under 35 U.S.C. § 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. § 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 53-61 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In the case *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case,

The nature of the invention

The nature of the invention of **Claims 53-61** is the use of an agent comprising a compound according to Formula (III) for the treatment and/or prevention of immunological diseases, inflammatory diseases, neurodegenerative diseases, or metabolic diseases.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the

art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the claimed invention is highly unpredictable since one skilled in the art would recognize that although a composition comprising a compound according to Formula (III) may exhibit excellent JNK inhibitory action, the state of the art is such that exhibiting excellent JNK inhibitory action does not necessarily conclude that the compositions are useful for the treatment or prevention of immunological diseases, inflammatory diseases, neurodegenerative diseases, or metabolic diseases. Described in the Specification on page 7 is the only known pyrazole derivative, and therefore the only known example of a compound in the same class as the instantly claimed compounds, having JNK inhibitory effect. Although it has been determined that compounds having inhibitory effect on JNK pathway *may be expected* to be useful as therapeutic drugs for the treatment of immunological diseases, inflammatory diseases, neurodegenerative diseases, or metabolic diseases; this is not been demonstrated with an analogous compound (same class: i.e. pyrazole) to be true at the time of filing.

The level of the skill in the art & the quantity of experimentation needed

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which agents exhibit the desired pharmacological activity.

Thus, the specification fails to provide sufficient support for the broad use of compounds and compositions according to formula (III) for the treatment and/or prevention of immunological diseases, inflammatory diseases, neurodegenerative diseases, or metabolic diseases. As a result, one of skill in the art would be required to perform an exhaustive clinical trial to determine the link between what is known: a composition comprising a compound according to Formula (III) may exhibit excellent JNK inhibitory action; and what is unknown: if a composition comprising a compound according to Formula (III) is useful for the treatment and/or prevention of immunological diseases, inflammatory diseases, neurodegenerative diseases, or metabolic diseases.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 states, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 20, 22, 23 and 50 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over **Claims 20, 22, 23, and 50** of copending Application No. **10/447,948**. Although the conflicting claims are not identical, there is nearly 100% overlap between said claims. Therefore, a reference or case of infringement that anticipates or renders obvious the claims of one application may also anticipate or render obvious the claims of the other application. Furthermore, both applications are drawn to compounds and compositions of the formula (III), which have been found useful for the inhibition of the JNK kinases. Therefore, one of ordinary skill in the art when faced with copending application

10/447,948 would be motivated to prepare applicants' instant elected invention as the conflicting claims generically encompass nearly 100% of the instantly claimed application for patent. The motivation would be to prepare additional compounds for the inhibition of JNK kinases. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Objections

Claims 21 and 49 are objected to as being dependent upon rejected base **Claim 20**, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 51 and 52 are objected to under 37 CFR 1.75 as being a substantial duplicate of **Claim 50.** When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jason M. Nolan, Ph.D.** whose telephone number is **(571) 272-4356** and electronic mail is **Jason.Nolan@uspto.gov**. The examiner can normally be reached on Mon - Fri (9:00 - 5:30PM). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph M^{c}Kane** can be reached on **(571) 272-0699**. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jason M. Nolan, Ph.D.
Examiner
Art Unit 1626

/- Joseph K. M^{c}Kane
Supervisory Patent Examiner
Art Unit 1626
Date: September 13, 2006